

Effect of Depression on Serum Levels of Follicular Stimulating Hormone and Luteinizing Hormone in Male Population of Military Hospital, Rawalpindi

Nasar Abbas Shamsi¹, Shazia Ali², Shazadi Ambreen³, Hira Ayaz⁴, Sobia Waqas⁵, Sidra Arshad⁶

^{1,4}Assistant Professor, Physiology, Foundation University Islamabad, Pakistan.

²Professor, Physiology, Islamic International Medical College, Islamabad, Pakistan.

³Senior Lecturer, Physiology, Shifa Tameer e Millat University Islamabad, Pakistan

⁵Assistant Professor, Physiology, Fazaia Medical College Islamabad, Pakistan.

⁶Associate Professor, Physiology, Rawal Institute of Health Sciences, Islamabad, Pakistan.

ABSTRACT

Background: Depression is a psychiatric illness that affects the overall life quality of an individual. In depression along with other symptoms, one of the features affecting the personal life of individuals is loss of libido which is influenced by the hypothalamic-pituitary-testicular axis. This study was aimed to determine the serum levels of Follicular stimulating hormone (FSH) and Luteinizing hormone (LH) in depressed male patients.

Methodology: This comparative cross sectional study was done at Islamic International Medical College and Armed Forces Institute of Mental Health, Military Hospital Rawalpindi after being approved by ethical review committee. After informed consent, 96 male individuals having 18 – 60 years of age participated in the current study. Participants were segregated into groups A and B. Gender and age-matched healthy subjects in a quantity of 24 were taken in group A whereas group B consisted of 72 male depressed patients. Serum gonadotropins levels of both groups were compared by using an independent student t-test in SPSS 21.

Results: Serum FSH (2.66 ± 0.34 mIU/ml) and LH (2.67 ± 0.18 mIU/ml) levels of Group A have shown no significant difference as compared to serum FSH (3.32 ± 0.43 mIU/ml) and LH (3.12 ± 0.19 mIU/ml) levels of Group B.

Conclusion: It is concluded from the study that serum FSH and LH levels were not significantly decreased in individuals with depression.

Keywords: Depression, Follicle stimulating hormone, Luteinizing hormone

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{3,4}Critical analysis and manuscript review; ^{5,6}Data analysis; Manuscript Editing.

Correspondence:

Nasar Abbas Shamsi
Email: n.abbas@fui.edu.pk

Article info:

Received: October 19, 2021
Accepted: December 27, 2022

Cite this article. Shamsi N A, Ali S, Ambreen S, Ayaz H, Waqas S, Arshad S. Effect of Depression on Serum Levels of Follicular Stimulating Hormone and Luteinizing Hormone in Male Population of Military Hospital, Rawalpindi. J Islamabad Med Dental Coll. 2022; 11(4): 216-221

Funding Source: Nil

Conflict of Interest: Nil

DOI: <https://doi.org/10.35787/jimdc.v11i4.797>

Introduction

Depression is a psychiatric illness which has deleterious effects on feelings, thought process and

overall behavior of an individual¹. In depression, cognitive and behavioral abnormalities are accompanied by an important manifestation which

is the loss of sexual desire and challenges to maintain intimate sexual relationships². Reduced sexual activity badly affects the individual's family life and leads to severe Depression which ultimately hindered the management of illness. The complex neuroendocrine network of hypothalamic pituitary testicular axis plays a central role in controlling the sexual activities of an individual³.

The hypothalamus plays a pivotal role in hypothalamic-pituitary-testicular axis by secreting gonadotropin-releasing hormone (GnRH) which will affect the secretions of pituitary gland³. GnRH is a decapeptide synthesized by specialized neurons of the arcuate nucleus and preoptic area of hypothalamus⁴. Pathologies involving hypothalamus especially those having underlying dysfunction of hypothalamic pituitary adrenal axis and suprachiasmatic nucleus have been seen to be involved in the development of mood disorders⁵.

Release of GnRH in pulsatile form by the hypothalamus will cause stimulation of pituitary gland which will ultimately secrete Follicle stimulating hormone (FSH) and Luteinizing hormone (LH)^{6,7}.

Upon binding of FSH to its receptors in testis, there will be release of factors like P-450 aromatase, Growth factors, Inhibin and Androgen-binding protein (ABP) along with Anti-mullerian hormone from the sertoli cells of testes. Synthesis and action of certain steroid hormones is dependent on these factors⁸. Antimullerian hormone released from testes promotes brain development and cognition⁹. LH released from Pituitary gland causes Testosterone production in males¹⁰. A wide range of functions in males is exerted by Testosterone which includes spermatogenesis, secondary sexual traits development and behavioral characteristics like sexual motivation, libido and aggression¹¹. In addition, testosterone is also important for brain development and cognitive processes of the brain¹². FSH and LH are also associated with central nervous system functions like regulation of cognition and

mood. Low levels of FSH and LH have been observed in diseases that affect the cognitive behavior of an individual^{13, 14}. It has also been observed that the response of gonadotropins to GnRH is reduced in case of psychiatric illness like depression and mood disturbances¹⁵.

The present research is planned to determine FSH and LH levels in serum of male individuals with depression which can be considered while addressing treatment protocol for patients.

Methodology

This comparative cross sectional study was conducted in Islamic International Medical College in collaboration with Armed Forces Institute of Mental Health, from 2nd January 2018 to 23rd April after approval by the Ethical Review Committee.

Informed consent was taken from 96 males which were considered to be participating in the study. Age of these males was from 18 to 60 years. Sample size was calculated by taking prevalence 4.2 % of depression using Raosoft sample size calculator at 95% confidence level and standard error 5%¹⁶. Two groups were made from participants. Group A, comprised of age-matched 24 healthy male individuals without depression while Group B, comprised of 76 patients with depression diagnosed by using the Siddiqui Shah Depression Scale (SSDS). The SSDS was developed by Dr. Salma Siddiqui and Dr. Syed Ashiq Ali Shah and it consists of 36 items in which each item can be scored from 0-4 with range of total scores of 0-108. Scores of 26 or above is considered to be an indication of Depressive illness¹⁷.

Inclusion criteria includes male gender, body mass index (BMI) < 30 with no chronic illness or physical anomaly. Individuals with depression but under Electroconvulsive therapy (ECT), alcohol or drug abusers, having BMI >30, and patients with other obvious physical deformities and chronic illness were not included in the current study.

Body Mass Index (BMI) and age of all participants

along with the duration of illness of depressive individuals was recorded. Blood sampling was done from medial cubital veins by considering aseptic measures. Separated serum obtained after centrifugation at 3000 RMP for 10 minutes was stored at the temperature of -20 °C. Serum Gonadotropins (Follicular stimulating hormone and Luteinizing hormone) levels were determined by ELISA Kits which are manufactured by *Bios USA*. Analysis of data was done with the help of Statistical Package for Social Sciences version 21 (SPSS 21). All the results deduced were reported in the form of mean \pm SEM. Serum gonadotropins (ng/ml) levels of Group A and Group B were compared by employing Independent sample t-test. p-value of ≤ 0.05 was considered as significant.

Results

In this study, 96 male participants were divided into 2 different groups: Group A and B. Group A served as the control group while Group B was having diagnosed patients with depression.

Table 1 is depicting the Age and Body mass index (BMI) of all participants. Comparison of Mean \pm SEM

of the age of Group A (34.12 ± 1.49 years) and Group B (35.19 ± 1.18 years) showed no significant difference. Mean \pm SEM of BMI of Group A (25.02 ± 0.23) was compared with that of Group B (23.85 ± 0.25) and no significant difference was observed. 1.60 ± 0.17 years was the duration of depression of group B.

Parameter	Group A (Controls) (n=24)	Group B (Depressed patients) (n=72)
Age (years)	34.12 ± 1.49	35.19 ± 1.18
Body Mass Index (BMI)	25.02 ± 0.23	23.85 ± 0.25
Duration of disease (years)	-	1.60 ± 0.17

Serum Follicle-stimulating hormone levels (mIU/ml)

No significant difference ($p = 0.39$) was observed on comparing Follicle-stimulating hormone (FSH) levels (mIU/ml) of group A (2.66 ± 0.34 mIU/ml) with FSH levels of Group B (3.32 ± 0.43 mIU/ml). Serum FSH levels of Group A and B are shown in Graph 1.

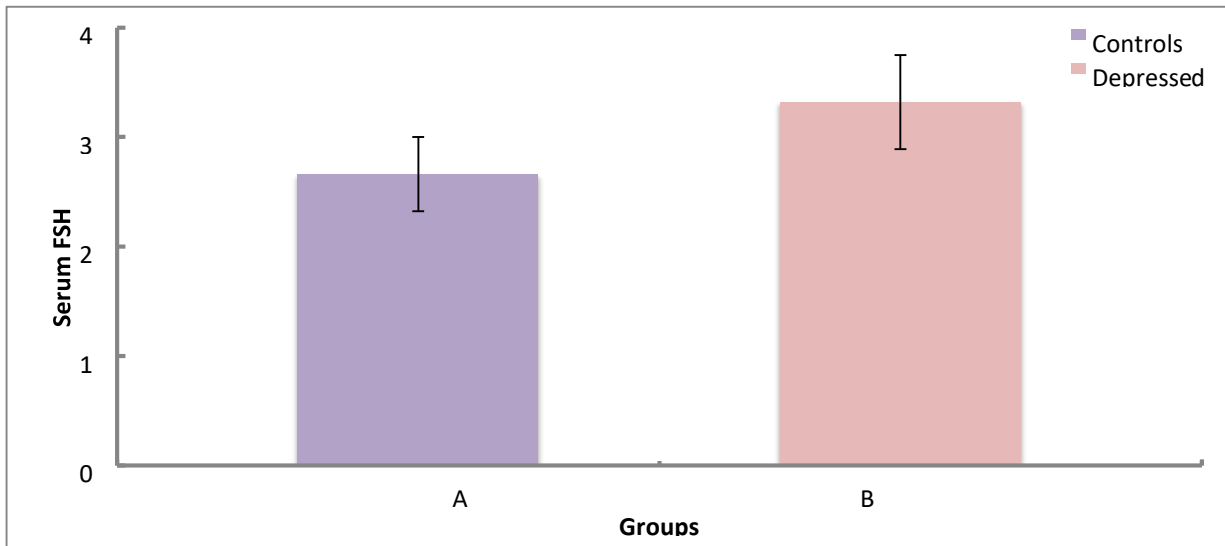


Figure 1: Comparison of Mean \pm SEM of serum FSH levels (mIU/ml) of Group A (Controls) with Group B (Depressed male patients). $P < 0.05$ was considered significant in statistical analysis.

Serum Luteinizing hormone levels (mIU/ml)

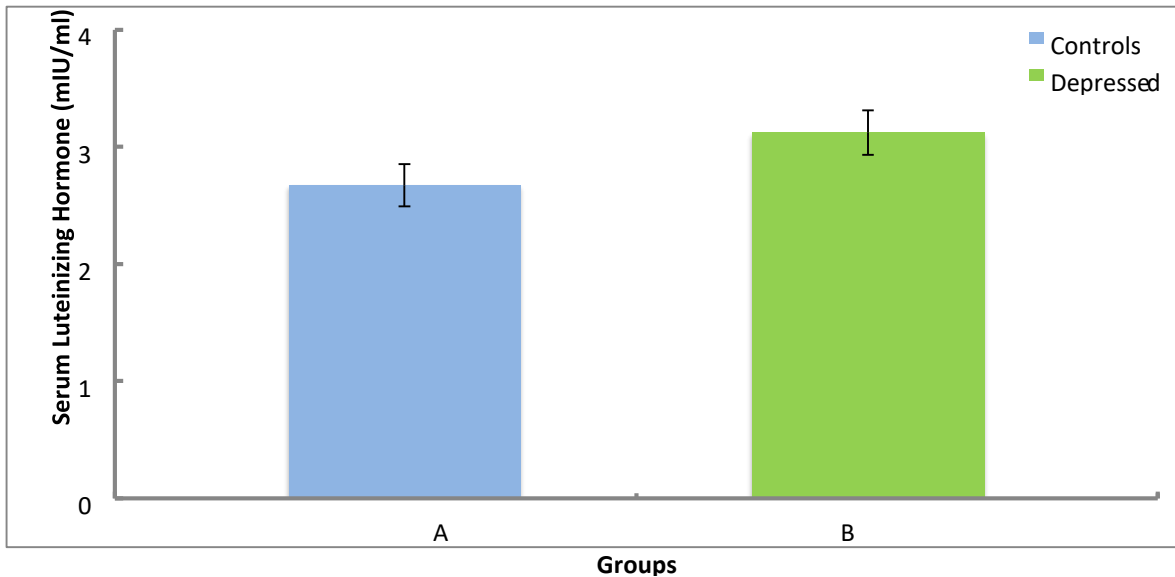


Figure II: Comparison of Mean \pm SEM of serum LH levels (mIU/ml) of Group A (Controls) with Group B (Depressed male patients). $P < 0.05$ was considered statistically significant.

Discussion

This research project was planned out to evaluate the association of gonadotropins with Depression in male patients.

We have inferred from data of the present study that there is no significant variation in serum FSH and LH levels in Depressive male individuals as compared to healthy individuals which are in concurrence to findings of a prospective cohort study conducted by Prasad et al. in which they included normal women having age of 18-44 years and observed that FSH and LH concentration in women having or not having depressive symptoms had shown no significant difference¹⁸. Observation made in another study was contrary to our results. In their study, they incorporated the women who came for follow-up at 6 weeks after delivery and they observed female individuals with postpartum depression had increased levels of serum FSH levels, decreased levels of serum LH, and low LH/FSH ratio¹⁹. A study was done on females with major depressive disorder (MDD) to explore the link between suicide and hormones of the female

reproductive system²⁰. They observed significantly lower levels of serum FSH in MDD patients having suicidal ideation or attempt in comparison to MDD patients not having these types of ideations or attempts. They concluded that FSH may serve as a biological indicator of current suicidality. These findings are contrary to our results but it could be due to the reason that none of our patients was having suicidal ideations or reported suicidal attempts. Another study demonstrated that no statistically significant difference was present in serum FSH and LH levels of males having age 50-70 years with and without depressive symptoms which is in accordance with our findings²¹. In a meta-analysis, seventeen studies were identified and reviewed to know about the status of hormones of the hypothalamic-pituitary-gonadal (HPG) axis in male patients of depression which showed that FSH and LH did not differ between patients and controls²².

Conclusion

In brief, it is obvious from the outcomes of the present study that FSH and LH were different in depressive male patients as compared to healthy individuals but this dissimilarity was not significant statistically. However this fact cannot be ignored that all patients included in our project were already taking the treatment for depression. In order to validate the results patients without antidepressants treatment should be included.

Recommendations

Newly diagnosed Depressive patients without treatment may be included in further studies. In future, studies involving the magnetic resonance imaging (MRI) can be carried out for analysis of the hippocampal volume. Estimation of gonadotropin-releasing hormone (GnRH) may be considered to have a better understanding of hypothalamic-pituitary-testicular axis and neurogenesis in Depression.

REFERENCES

1. Lima IMM, Peckham AD, Johnson SL. Cognitive deficits in bipolar disorders: Implications for emotion. *Clin Psychol Rev.* 2018;59:126-36. doi: 10.1016/j.cpr.2017.11.006.
2. Steinke EE, Mosack V, Hill TJ. Depression, Quality of Life, Physical Activity, and the Impact of Drugs on Sexual Activity in a Population-Based Sample, Ages 20-59 Years. *Issues Ment Health Nurs.* 2018;39(6):527-32. doi: 10.1080/01612840.2017.1413463.
3. Kaprara A, Huhtaniemi IT. The hypothalamus-pituitary-gonad axis: tales of mice and men. *Metabolism.* 2018;86:3-17. doi: 10.1016/j.metabol.2017.11.018.
4. Cimino I, Casoni F, Liu X, Messina A, Parkash J, Jamin SP, et al. Novel role for anti-Müllerian hormone in the regulation of GnRH neuron excitability and hormone secretion. *Nat Commun.* 2016;7(1):1-12. doi: 10.1038/ncomms10055.
5. Bao AM, Swaab DF. The human hypothalamus in mood disorders: The HPA axis in the center. *IBRO Rep.* 2019;6:45-53. doi: 10.1016/j.ibror.2018.11.008.
6. Lunenfeld B, Bühler K. The neuro control of the ovarian cycle - a hypothesis. *Gynecol Endocrinol.* 2018;34(4):278-82. doi: 10.1080/09513590.2017.1405933.
7. Plant DT, Pariante CM, Sharp D, Pawlby S. Maternal depression during pregnancy and offspring depression in adulthood: role of child maltreatment. *Br J Psychiatry.* 2015;207(3):213-20. doi: 10.1192/bjp.bp.114.156620.
8. Bhattacharya I, Basu S, Pradhan BS, Sarkar H, Nagarajan P, Majumdar SS. Testosterone augments FSH signaling by upregulating the expression and activity of FSH-Receptor in Pubertal Primate Sertoli cells. *Mol Cell Endocrinol.* 2019;482:70-80. doi:10.1016/j.mce.2018.12.012.
9. Morgan K, Ruffman T, Bilkey DK, McLennan IS. Circulating anti-Müllerian hormone (AMH) associates with the maturity of boys' drawings: Does AMH slow cognitive development in males? *Endocrine.* 2017;57(3):528-34. doi: 10.1007/s12020-017-1333-2.
10. O'Hara L, Curley M, Tedim Ferreira M, Cruickshanks L, Milne L, Smith LB. Pituitary androgen receptor signalling regulates prolactin but not gonadotrophins in the male mouse. *PLoS One.* 2015;10(3):e0121657. doi: 10.1371/journal.pone.0121657.
11. Celec P, Ostatníková D, Hodosy J. On the effects of testosterone on brain behavioral functions. *Front Neurosci.* 2015;9:12. doi: 10.3389/fnins.2015.00012.
12. Corona G, Guaraldi F, Rastrelli G, Sforza A, Maggi M. Testosterone Deficiency and Risk of Cognitive Disorders in Aging Males. *World J Mens Health.* 2021;39(1):9-18. doi: 10.5534/wjmh.200017.
13. Crawford ED, Schally AV, Pinthus JH, Block NL, Rick FG, Garnick MB, et al. The potential role of follicle-stimulating hormone in the cardiovascular, metabolic, skeletal, and cognitive effects associated with androgen deprivation therapy. *Urol Oncol.* 2017;35(5):183-91. doi: 10.1016/j.urolonc.2017.01.025.
14. Kim GW, Park K, Jeong GW. Effects of Sex Hormones and Age on Brain Volume in Post-Menopausal Women. *J Sex Med.* 2018;15(5):662-70. doi: 10.1016/j.jsxm.2018.03.006.
15. Henningsson S, Madsen KH, Pinborg A, Heede M, Knudsen GM, Siebner HR, et al. Role of emotional processing in depressive responses to sex-hormone manipulation: a pharmacological fMRI study. *Transl Psychiatry.* 2015;5(12):e688. doi: 10.1038/tp.2015.184.
16. Raosoft I. Sample size calculator by Raosoft, Inc
17. Siddiqui S, Ali Shah SA. Siddiqui-shah depression scale (SSDS): development and validation. *Psychology and developing societies.* 1997 Sep;9(2):245-62. doi:10.1177/097133369700900205.
18. Prasad A, Schisterman EF, Schliep KC, Ahrens KA, Sjaarda LA, Perkins NJ, et al. Depressive symptoms and their relationship with endogenous reproductive hormones and sporadic anovulation in premenopausal women. *Ann Epidemiol.* 2014;24(12):920-4. doi: 10.1080/09513590.2017.1405933.

- 10.1016/j.annepidem.2014.10.005.
19. Ramachandran Pillai R, Sharon L, Premkumar NR, Kattimani S, Sagili H, Rajendiran S. Luteinizing hormone-follicle stimulating hormone ratio as biological predictor of post-partum depression. *Compr Psychiatry*. 2017;72:25-33. doi: 10.1016/j.comppsy.2016.09.001.
 20. Kim B, Kang ES, Fava M, Mischoulon D, Soskin D, Yu BH, et al. Follicle-stimulating hormone (FSH), current suicidal ideation and attempt in female patients with major depressive disorder. *Psychiatry Res*. 2013;210(3):951-6. doi: 10.1016/j.psychres.2013.08.057.
 21. Liu ZY, Zhou RY, Lu X, Zeng QS, Wang HQ, Li Z, et al. Identification of late-onset hypogonadism in middle-aged and elderly men from a community of China. *Asian J Androl*. 2016;18(5):747-53. doi: 10.4103/1008-682X.160883.
 22. Fischer S, Ehlert U, Castro RA. Hormones of the hypothalamic-pituitary-gonadal (HPG) axis in male depressive disorders—A systematic review and meta-analysis. *Frontiers in Neuroendocrinology*. 2019 Oct 1;55:100792. doi: 10.1016/j.yfrne.2019.100792.